THE 19 700 PER THANK THA

110> Glaxo Group Ltd Tate, Simon N Delany, Natalie S Sanseau, P

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<150> GB 9826359.3

<151> 1998-12-01

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<170> PatentIn Ver. 2.1

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969

131

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ser	GIn		Ser	Val	Ala	Ala	Ser	Thr	Glu	Lys	Thr		Arg	Leu	Tyr	
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Аър	115	Arg	ser	116	Pne	120	Ala	vai	АТА	GIN		ASN	Cys	GIN	Asp	
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Ile	Glu	Arg	Arg	Asn	Met	Ala	Leu	Val	Thr	Leu	Leu	Val	Glu	Asn	Gly	
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Gly	Arg	Pro	Gly	Phe	Tyr	Phe	Gly	Glu	Leu	Pro	Leu	Ser	Leu	Ala	Ala	
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Cys	Thr		GIn	Leu	Gly	Ile	Val	Lys	Phe	Leu	Leu		Asn	Ser	Trp	
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a	200	~~~							•							
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GIII	275	Ата	Asp	тте	ser		Arg	Asp	ser	vaı		Asn	Tnr	vaı	Leu	
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ccg	acg	ctg	aag	ctg	gag	gag	ctc	acc	aac	aag	aag	gga	atg	acg	ccg	1785
Pro	Thr	Leu	Lys	Leu	Glu	Glu	Leu	Thr	Asn	Lys	Lys	Gly	Met	Thr	Pro	
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Leu	Ala	Leu	Ala	Ala	Gly	Thr	Gly	Lys	Ile	Gly	Val	Leu	Ala	Tyr	Ile	
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Leu	Gln	Arg	Glu	Ile	Gln	Glu	Pro	Glu	Cys	Arg	His	Leu	Ser	Arg	Lys	
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	Thr	Glu	Trp	Ala	Tyr	Gly	Pro	Val	His	Ser	Ser	Leu	Tyr	Asp	Leu	
370					375			•		380					385	
tee	taa	250	~~~											ì		
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Pro	Leu	Asn	Arg	Leu	Leu	Gln	Asp	Lys	Trp	Asp	Arg	Phe	Val	Lys	Arg	
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Ile	Phe	Tyr	Phe	Asn	Phe	Leu	Val	Tyr	Cys	Leu	Tyr	Met	Ile	Ile	Phe	
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	Met	Ala	Ala	Tyr	Tyr	Arg	Pro	Val	Asp		Leu	Pro	Pro	Phe		
450					455					460					465	
ata	<i>α</i>	222	a++	~~~	~~~				~	~~+		~~~			+	2217
					gac Asp											2211
ricc	Olu	цуб	116	470	мър	ıyı	FIIC	Arg	475	1111	GIY	Giu	116	480	361	
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gtq	tta	qqa	qqa	qtc	tac	ttc	ttt	ttc	саа	qaa	att	caq	tat	ttc	cta	2265
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BI

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Gln	Arg	Arg	Pro	Ser	Met	Lys	Thr	Leu	Phe	Val	Asp	Ser	Tyr	Ser	Glu	
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Met	Leu	Phe	Phe	Leu	Gln	Ser	Leu	Phe	Met	Leu	Ala	Thr	Val	Val	Leu	
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tac	ttc	agc	cac	ctc	aag	gag	tat	gtg	gct	tcc	atg	gta	ttc	tcc	ctg	2409
Tyr	Phe	Ser	His	Leu	Lys	Glu	Tyr	Val	Ala	Ser	Met	Val	Phe	Ser	Leu	
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Ala	Leu	Gly	Trp	Thr	Asn	Met	Leu	Tyr	Tyr	Thr	Arg	Gly	Phe	Gln	Gln	
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Met	Gly	Ile	Tyr	Ala	Val	Met	Ile	Glu	Lys	Met	Ile	Leu	Arg	Asp	Leu	
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tgc	cgt	ttc	atg	ttt	gtc	tac	atc	gtc	ttc	ttg	ttc	ggg	ttt	tcc	aca	2553
Cys	Arg	Phe	Met	Phe	Val	Tyr	Ile	Val	Phe	Leu	Phe	Gly	Phe	Ser	Thr	
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gcg	gtg	gtg	acg	ctg	att	gaa	gac	999	aag	aat	gac	tcc	ctg	ccg	tct	2601
Ala	Val	Val	Thr	Leu	Ile	Glu	Asp	Gly	Lys	Asn	Asp	Ser	Leu	Pro	Ser	
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gag	tcc	acg	tcg	cac	agg	tgg	cgg	aaa	cct	gcc	tgc	agg	ccc	ccc	gat	2649
Glu	Ser	Thr	Ser	His	Arg	Trp	Arg	Gly	Pro	Ala	Cys	Arg	Pro	Pro	Asp	
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agc	tcc	tac	aac	agc	ctg	tac	tcc	acc	tgc	ctg	gag	ctg	ttc	aag	ttc	2697
Ser	Ser	Tyr	Asn	Ser	Leu	Tyr	Ser	Thr	Cys	Leu	Glu	Leu	Phe	Lys	Phe	
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Arg His Trp Lys Asn Phe Ala Leu Val Pro Leu Leu Arg Glu Ala Ser
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gct cga gat agg cag tct gct cag ccc gag gaa gtt tat ctg cga cag 3225
Ala Arg Asp Arg Gln Ser Ala Gln Pro Glu Glu Val Tyr Leu Arg Gln
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ttt tca ggg tct ctg aag cca gag gac gct gag gtc ttc aag agt cct 3273

Phe Ser Gly Ser Leu Lys Pro Glu Asp Ala Glu Val Phe Lys Ser Pro
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Ala Ala Ser Gly Glu Lys

835

BI

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Gln Lys Asp Thr Cys Pro Asp Pro Leu Asp Gly Asp Pro Asn Ser Arg
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Pro Pro Pro Ala Lys Pro Gln Leu Ser Thr Ala Lys Ser Arg Thr Arg 35 40 45

Leu Phe Gly Lys Gly Asp Ser Glu Glu Ala Phe Pro Vàl Asp Cys Pro
50 55 60

His Glu Glu Gly Glu Leu Asp Ser Cys Pro Thr Ile Thr Val Ser Pro 65 70 75 80

Val	Ile	Thr	Ile	Gln	Arg	Pro	Gly	Asp	Gly	Pro	Thr	Gly	Ala	Arg	Let
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Leu	Ser	Gln	Asp	Ser	Val	Ala	Ala	Ser	Thr	Glu	Lys	Thr	Leu	Arg	Let
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Tyr	Asp	Arg	Arg	Ser	Ile	Phe	Glu	Ala	Val	Ala	Gln	Asn	Asn	Cys	Glr
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Asp	Leu	Glu	Ser	Leu	Leu	Leu	Phe	Leu	Gln	Lys	Ser	Lys	Lvs	His	Leu
	130					135				2	140	4 ·-			
Thr	Asp	Asn	Glu	Phe	Lvs	Asp	Pro	Glu	Thr	Glv	Lvs	Thr	Cvs	Len	Lei
145	F				150			014	****	155	2,5		Cyb	Dea	160
113					130					133					100
Tare	ח ה	Mot	T 011	7.00	Tou	TI i a	7 ~~	a 1	01 =	3	mb	mb	T] -	Deep	T
пуъ	Ala	Mec	Leu		ьeu	HIS	Asp	GIY		Asn	Thr	Thr	ше		ьет
				165					170					175	
_				_											
Leu	Leu	Glu	Ile	Ala	Arg	Gln	Thr		Ser	Leu	Lys	Glu	Leu	Val	Asr
			180					185					190		
Ala	Ser	Tyr	Thr	Asp	Ser	Tyr	Tyr	Lys	Gly	Gln	Thr	Ala	Leu	His	Il€
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Ala	Ile	Glu	Arg	Arg	Asn	Met	Ala	Leu	Val	Thr	Leu	Leu	Val	Glu	Asr
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Gly	Ala	Asp	Val	Gln	Ala	Ala	Ala	His	Gly	Asp	Phe	Phe	Lys	Lys	Thr
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Lys	Glv	Ara	Pro	Glv	Phe	Tvr	Phe	Glv	Glu	Leu	Pro	Leu	Ser	Leu	Ala
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Ala Cys Thr Asn Gln Leu Gly Ile Val Lys Phe Leu Leu Gln Asn Ser
260 265 270

Trp Gln Thr Ala Asp Ile Ser Ala Arg Asp Ser Val Gly Asn Thr Val
275 280 285

Leu		Ala	Leu	Val	Glu		Ala	Asp	Asn	Thr		Asp	Asn	Thr	Lys
Dho	290	Th.~	C.~	M∽►	Т.	295	03	T7 -	T	T7 -	300	a 1	77 -	T	T
	val	inr	ser	Met		ASN	GIU	тте	Leu		ьeu	GIY	Ala	ьуѕ	
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His	Pro	Thr	Leu	Lys	Leu	Glu	Glu	Leu	Thr	Asn	Lys	Lys	Gly	Met	Thr
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Pro	Leu	Ala	Leu	Ala	Ala	Gly	Thr	Gly	Lys	Ile	Gly	Val	Leu	Ala	Tyr
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Ile	Leu	Gln	Arg	Glu	Ile	Gln	Glu	Pro	Glu	Cys	Arg	His	Leu	Ser	Arg
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Leu	Ser	Cys	Ile	Asp	Thr	Cys	Glu	Lys	Asn	Ser	Val	Leu	Glu	Val	Ile
385					390					395					400
Ala	Tyr	Ser	Ser	Ser	Glu	Thr	Pro	Asn	Arg	His	Asp	Met	Leu	Leu	Val
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	_	_	_	_		_					_			-	_
GIu	Pro	Leu		Arg	Leu	Leu	Gln		Lys	Trp	Asp	Arg		Val	Lys
			420					425					430		
λra	Tle	Dhe	Ф. т.	Dho	7 an	Dho	T 011	v. l	TT	Crra	Ton	TT	Mot	Tle	Tle
Arg	116	435	IYL	PIIC	ASII	Pne		vaı	Tyr	Cys	ьeu	1 y I 4 4 5	MEC	116	116
	ė	433					440					443			
Phe	Thr	Met	Δla	Δla	ጥ _ህ ዮ	Tvr	Ara	Pro	Val	Δsn	Glv	Len	Pro	Pro	Phe
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	-50										100				
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Ser Val Leu Gly Gly Val Tyr Phe Phe Phe Arg Gly Ile Gln Tyr Phe



Leu Gln Arg Arg Pro Ser Met Lys Thr Leu Phe Val Asp Ser Tyr Ser 500 505 510

Glu Met Leu Phe Phe Leu Gln Ser Leu Phe Met Leu Ala Thr Val Val 515 520 525

Leu Tyr Phe Ser His Leu Lys Glu Tyr Val Ala Ser Met Val Phe Ser 530 540

Leu Ala Leu Gly Trp Thr Asn Met Leu Tyr Tyr Thr Arg Gly Phe Gln 545 550 555 560

Gln Met Gly Ile Tyr Ala Val Met Ile Glu Lys Met Ile Leu Arg Asp
565 570 575

Leu Cys Arg Phe Met Phe Val Tyr Ile Val Phe Leu Phe Gly Phe Ser 580 585 590

Thr Ala Val Val Thr Leu Ile Glu Asp Gly Lys Asn Asp Ser Leu Pro 595 600 605

Ser Glu Ser Thr Ser His Arg Trp Arg Gly Pro Ala Cys Arg Pro Pro 610 620

Asp Ser Ser Tyr Asn Ser Leu Tyr Ser Thr Cys Leu Glu Leu Phe Lys 625 630 635 640

Phe Thr Ile Gly Met Gly Asp Leu Glu Phe Thr Glu Asn Tyr Asp Phe 645 650 655

Lys Ala Val Phe Ile Ile Leu Leu Leu Ala Tyr Val Ile Leu Thr Tyr 660 665 670

Ile Leu Leu Leu Asn Met Leu Ile Ala Leu Met Gly Glu Thr Val Asn 675 680 685

Lys Ile Ala Gln Glu Ser Lys Asn Ile Trp Lys Leu Gln Arg Ala Ile 690 695 700

Thr Ile Leu Asp Thr Glu Lys Ser Phe Leu Lys Cys Met Arg Lys Ala
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Phe Arg Ser Gly Lys Leu Leu Gln Val Gly Tyr Thr Pro Asp Gly Lys
725 730 735

Asp Asp Tyr Arg Trp Cys Phe Arg Val Asp Glu Val Asn Trp Thr Thr
740 745 750

Trp Asn Thr Asn Val Gly Ile Ile Asn Glu Asp Pro Gly Asn Cys Glu
755 760 765

Gly Val Lys Arg Thr Leu Ser Phe Ser Leu Arg Ser Ser Arg Val Ser
770 780

Gly Arg His Trp Lys Asn Phe Ala Leu Val Pro Leu Leu Arg Glu Ala
785 790 795 800

Ser Ala Arg Asp Arg Gln Ser Ala Gln Pro Glu Glu Val Tyr Leu Arg 805 810 815

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Ser Tyr Thr Asp Ser Tyr Tyr Lys Gly Gln Thr Ala Leu His Ile Ala

195	200	205
	200	205

Ile Glu Arg Arg Asn Met Thr Leu Val Thr Leu Leu Val Glu Asn Gly
210 220

Ala Asp Val Gln Ala Ala Ala Asn Gly Asp Phe Phe Lys Lys Thr Lys
225 230 235 240

Gly Arg Pro Gly Phe Tyr Phe Gly Glu Leu Pro Leu Ser Leu Ala Ala 245 250 255

Cys Thr Asn Gln Leu Ala Ile Val Lys Phe Leu Leu Gln Asn Ser Trp
260 265 270

Gln Pro Ala Asp Ile Ser Ala Arg Asp Ser Val Gly Asn Thr Val Leu 275 280 285

His Ala Leu Val Glu Val Ala Asp Asn Thr Val Asp Asn Thr Lys Phe 290 295 300

Val Thr Ser Met Tyr Asn Glu Ile Leu Ile Leu Gly Ala Lys Leu His 305 310 315 320

Pro Thr Leu Lys Leu Glu Glu Ile Thr Asn Arg Lys Gly Leu Thr Pro 325 330 335

Leu Ala Leu Ala Ser Ser Gly Lys Ile Gly Val Leu Ala Tyr Ile 340 345 350

Leu Gln Arg Glu Ile His Glu Pro Glu Cys Arg His Leu Ser Arg Lys 355 360 365

Phe Thr Glu Trp Ala Tyr Gly Pro Val His Ser Ser Leu Tyr Asp Leu 370 375 380

Ser Cys Ile Asp Thr Cys Glu Lys Asn Ser Val Leu Glu Val Ile Ala 385 390 395 400 Tyr Ser Ser Ser Glu Thr Pro Asn Arg His Asp Met Leu Leu Val Glu
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Pro Leu Asn Arg Leu Leu Gln Asp Lys Trp Asp Arg Phe Val Lys Arg
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Ile Phe Tyr Phe Asn Phe Phe Val Tyr Cys Leu Tyr Met Ile Ile Phe
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Thr Ala Ala Ala Tyr Tyr Arg Pro Val Glu Gly Leu Pro Pro Tyr Lys
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Ser Val Ser Gly Gly Val Tyr Phe Phe Phe Arg Gly Ile Gln Tyr Phe 485 490 495

Leu Gln Arg Arg Pro Ser Leu Lys Ser Leu Phe Val Asp Ser Tyr Ser 500 505 510

Glu Ile Leu Phe Phe Val Gln Ser Leu Phe Met Leu Val Ser Val Val
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Leu Tyr Phe Ser Gln Arg Lys Glu Tyr Val Ala Ser Met Val Phe Ser 530 535 540

Leu Ala Met Gly Trp Thr Asn Met Leu Tyr Tyr Thr Arg Gly Phe Gln 545 550 555 560

Gln Met Gly Ile Tyr Ala Val Met Ile Glu Lys Met Ile Leu Arg Asp
565 570 575

Leu Cys Arg Phe Met Phe Val Tyr Leu Val Phe Leu Phe Gly Phe Ser
580 585 590

Thr Ala Val Val Thr Leu Ile Glu Asp Gly Lys Asn Asn Ser Leu Pro 595 600 605



Met	Glu 610	Ser	Thr	Pro	His	Lys 615	Cys	Arg	Gly	Ser	Ala 620	Cys	Lys	Pro	Gly
Asn 625	Ser	Tyr	Asn	Ser	Leu 630	Tyr	Ser	Thr	Cys	Leu 635	Glu	Leu	Phe	Lys	Phe 640
				645					650					Phe 655	
Ala	Val	Phe	Ile 660	Ile	Leu	Leu	Leu	Ala 665	Tyr	Val	Ile	Leu	Thr 670	Tyr	Ile
Leu	Leu	Leu 675	Asn	Met	Leu	Ile	Ala 680	Leu	Met	Gly	Glu	Thr 685	Val	Asn	Lys
Ile	Ala 690	Gln	Glu	Ser	Lys	Asn 695	Ile	Trp	Lys	Leu	Gln 700	Arg	Ala	Ile	Thr
Ile 705	Leu	Asp	Thr	Glu	Lys 710	Ser	Phe	Leu	Lys	Cys 715	Met	Arg	Lys	Ala	Phe 720
Arg	Ser	Gly	Lys	Leu 725	Leu	Gln	Val	Gly	Phe 730	Thr	Pro	Asp	Gly	Lys 735	qzA
Asp	Tyr	Arg	Trp 740	Сув	Phe	Arg	Val	Asp 745	Glu	Val	Asn	Trp	Thr 750	Thr	Trp
Asn	Thr	Asn 755	Val	Gly	Ile	Ile	Asn 760	Glu	Asp	Pro	Gly	Asn 765	Cys	Glu	Gly
Val	Lys 770	Arg	Thr	Leu	Ser	Phe 775	Ser	Leu	Arg	Ser	Gly 780	Arg	Val	Ser	Gly
Arg 785	Asn	Trp	Lys	Asn	Phe 790	Ala	Leu	Val	Pro	Leu 795	Leu	Arg	Asp	Ala	Ser 800

Thr Arg Asp Arg His Ala Thr Gln Glu Glu Val Gln Leu Lys His



805

810

815

Tyr Thr Gly Ser Leu Lys Pro Glu Asp Ala Glu Val Phe Lys Asp Ser 820 825 830

Met Val Pro Gly Glu Lys 835

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cctgaagtcc accctcttc agcta atg ccc agg gta gtt gga cct ggg gcc 712

Met Pro Arg Val Val Gly Pro Gly Ala

1 5



aat ttg tgt ttc cag gtt cgt gaa aga ggc tcc tgt tgc agt tcc cgc Asn Leu Cys Phe Gln Val Arg Glu Arg Gly Ser Cys Cys Ser Ser Arg ctg agg ctg gcg gcc aac cac atc tgg gag tgg cct ccc tgt gcc cct Leu Arg Leu Ala Ala Asn His Ile Trp Glu Trp Pro Pro Cys Ala Pro gtc att aca acg gtg gct ttg aag cag ctg gca gca ctg ctg ctt gtc Val Ile Thr Thr Val Ala Leu Lys Gln Leu Ala Ala Leu Leu Val cac gtg gga ggg ggc ttc ctg gag ccc ccg ccc ctg gcc ggg ttc tgc His Val Gly Gly Phe Leu Glu Pro Pro Leu Ala Gly Phe Cys ctg act ccc ctt tca ttc cct tgc agg ctg agc agt gca gac ggg cct Leu Thr Pro Leu Ser Phe Pro Cys Arg Leu Ser Ser Ala Asp Gly Pro ggg gca ggc atg gcg gat tcc agc gaa ggc ccc cgc gcg ggg ccc ggg Gly Ala Gly Met Ala Asp Ser Ser Glu Gly Pro Arg Ala Gly Pro Gly gag gtg gct gag ctc ccc ggg gat gag agt ggc acc cca ggt ggg gag Glu Val Ala Glu Leu Pro Gly Asp Glu Ser Gly Thr Pro Gly Gly Glu gct ttt cct ctc tcc ctg gcc aat ctg ttt gag ggg gag gat ggc Ala Phe Pro Leu Ser Ser Leu Ala Asn Leu Phe Glu Gly Glu Asp Gly tcc ctt tcg ccc tca ccg gct gat gcc agt cgc cct gct ggc cca ggc Ser Leu Ser Pro Ser Pro Ala Asp Ala Ser Arg Pro Ala Gly Pro Gly

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Asp	Gly	Arg	Pro	Asn	Leu	Arg	Met	Lys	Phe	Gln	Gly	Ala	Phe	Arg	Lys	
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Lys	Ile	Ile	Glu	Lys	Gln	Pro	Gln	Ser	Pro	Lys	Ala	Pro	Ala	Pro	Gln	
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Pro	Pro	Pro	Ile	Leu	Lys	Val	Phe	Asn	Arg	Pro	Ile	Leu	Phe	Asp	Ile	
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Val	Ser	Arg	Gly	Ser	Thr	Ala	Asp	Leu	Asp	Gly	Leu	Leu	Pro	Phe	Leu	
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acg	999	aag	acc	tgc	ctg	ccc	aag	gcc	ttg	ctg	aac	ctg	agc	aat	ggc	1576
Thr	Gly	Lys	Thr	Cys	Leu	Pro	Lys	Ala	Leu	Leu	Asn	Leu	Ser	Asn	Gly	
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cgc	aac	gac	acc	atc	cct	gtg	ctg	ctg	gac	atc	gcg	gag	cgc	acc	ggc	1624
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aac	atg	cgg	gag	ttc	att	aac	tcg	ccc	ttc	cgt	gac	atc	tac	tat	cga	1672
Asn	Met	Arg	Glu	Phe	Ile	Asn	Ser	Pro	Phe	Arg	Asp	Ile	Tyr	Tyr	Arg	
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ggt	cag	aca	gcc	ctg	cac	atc	gcc	att	gag	cgt	cgc	tgc	aaa	cac	tac	1720
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410					415					420					425	
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Asn	Thr	Arg	Glu	Asn	Thr	Lys	Phe	Val	Thr	Lys	Met	Tyr	Asp	Leu	Leu	
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Leu	Lys	Cys	Ala	Arg	Leu	Phe	Pro	Asp	Ser	Asn	Leu	Glu	Ala	Val	
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Asn	Asn	Asp	Gly	Leu	Ser	Pro	Leu	Met	Met	Ala	Ala	Lys	Thr	Gly	
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Thr	Arg	His	Leu	Ser	Arg	Lys	Ser	Lys	Asp	Trp	Ala	Tyr	Gly	Pro	
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Tyr	Ser	Ser	Leu	Tyr	Asp	Leu	Ser	Ser	Leu	Asp	Thr	Cys	Gly	Glu	
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gcc	tcc	gtg	ctg	gag	atc	ctg	gtg	tac	aac	agc	aag	att	gag	aac	2296
Ala	Ser	Val	Leu	Glu	Ile	Leu	Val	Tyr	Asn	Ser	Lys	Ile	Glu	Asn	
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cac	gag	atg	ctg	gct	gtg	gag	ccc	atc	aat	gaa	ctg	ctg	cgg	gac	2344
His	Glu	Met	Leu	Ala	Val	Glu	Pro	Ile	Asn	Glu	Leu	Leu	Arg	Asp	
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Trp	Arg	Lys	Phe	Gly	Ala	Val	Ser	Phe	Tyr	Ile	Asn	Val	Val	Ser	
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Leu	Cys	Ala	Met	Val	Ile	Phe	Thr	Leu	Thr	Ala	Tyr	Tyr	Gln	Pro	
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Arg	Leu	Ala	Gly	Glu	Val	Ile	Thr	Leu	Phe	Thr	Gly	Val	Leu	Phe	Phe	
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Phe	Thr		Ile	Lys	Asp	Leu	Phe	Met	Lys	Lys	Cys	Pro	Gly	Val	Asn	
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Ser		Phe	Ile	Asp	Gly		Phe	Gln	Leu	Leu	Tyr	Phe	Ile	Tyr	Ser	
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	Leu	vaı	шe	Val		Ala	Ala	Leu	Tyr		Ala	Gly	Ile	Glu		
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							gcc									2728
TYL	пец	AIG	Mec	670	vai	PHE	Ala	Бец	675	пеп	Gry	пр	мес		Ата	
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	-1-	- 1.10	685	9	017	Lou	בענב	690		O _T y	****	-7-	695	110		
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Val	Phe	Leu	Arg	Lys	Ala	Phe	Arg	Ser	Gly	Glu	Met	Val	Thr	Val	Gly	
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Lys	Ser	Ser	Asp	Gly	Thr	Pro	Asp	Arg	Arg	Trp	Cys	Phe	Arg	Val	Asp	
		860					865					870				



Glu Val Asn Trp Ser His Trp Asn Gln Asn Leu Gly Tle Ile Asn Glu 875
gac ccg ggc aag aat gag acc tac cag tat tat ggc ttc tcg cat acc 3400 Asp Pro Gly Lys Asn Glu Thr Tyr Gln Tyr Gly Phe Ser His Thr 890
Asp Pro Gly Lys Asn Glu Thr Tyr Gln Tyr Gly Tyr Gly Phe Ser His Thr 890 Gly Gly Cr Cr 202 asp Cr Cr try Fro Cr Cr Gr 3448 910 Gly Arg Arg Arg Arg Trp Ser Ser Val Pro Arg Val 910 Gly Arg Arg Arg Trp Ser Ser Val Pro Arg Val Pro Arg Val Pro Arg Pro Arg Pro Arg Trp Ser Ser Val Val Pro Arg Val Pro Arg
Asp Pro Gly Lys Asn Glu Thr Tyr Gln Tyr Gly Tyr Gly Phe Ser His Thr 890 Gly Gly Cr Cr 202 asp Cr Cr try Fro Cr Cr Gr 3448 910 Gly Arg Arg Arg Arg Trp Ser Ser Val Pro Arg Val 910 Gly Arg Arg Arg Trp Ser Ser Val Pro Arg Val Pro Arg Val Pro Arg Pro Arg Pro Arg Trp Ser Ser Val Val Pro Arg Val Pro Arg
890
gtg ggc cgc ctc cgc agg gat cgc tgg tcc tcg gtg gtg gtg gtg gtg 3448 Val Gly Arg Leu Arg Arg Asp Arg Trp Ser Ser Val Val Pro Arg Val gtg gaa ctg aac tcg gac gag gtg gtg cct ctg 34496 Val Leu Asn Lys Asn Ser Asn Pro Asp Glu Val Val Val Pro Leu 3496 Val Leu Asn Lys Asn Ser Asn Pro Asp Glu Val Val Val Pro Leu 3496 gac agc atg ggg aac ccc cgc tgc cac cag cag ggt tac ccc 3544
Val Gly Arg Leu Arg Arg Asp Arg Trp Ser Ser Val Val Pro Arg Val gtg gaa ctg aac tcg aac ccg gac gag gtg gtg gtg cct ctg 3496 Val Glu Leu Asn Lys Asn Ser Asn Pro Asp Glu Val Val Val Pro Leu 3496 Val Leu Asn Lys Asn Ser Asn Pro Asp Glu Val Val Val Pro Leu Pro Leu Pro Leu Pro Leu Pro Leu Pro Pro Asp Ser Asp Gly His Gln Gly Tyr Pro Pro <td< td=""></td<>
Val Gly Arg Leu Arg Arg Asp Arg Trp Ser Ser Val Val Pro Arg Val gtg gaa ctg aac tcg aac ccg gac gag gtg gtg gtg cct ctg 3496 Val Glu Leu Asn Lys Asn Ser Asn Pro Asp Glu Val Val Val Pro Leu 3496 Val Leu Asn Lys Asn Ser Asn Pro Asp Glu Val Val Val Pro Leu Pro Leu Pro Leu Pro Leu Pro Leu Pro Pro Asp Ser Asp Gly His Gln Gly Tyr Pro Pro <td< td=""></td<>
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Val Glu Leu Asn Lys Asn Ser Asn Pro Asp Glu Val Val Pro Leu 930 935 935 935 935 935 936 936 936 935 936 936 936 936 936 936 936 936 936 936 936 936 936 936 940 945 940 940 940 945 940 9
Val Glu Leu Asn Lys Asn Ser Asn Pro Asp Glu Val Val Pro Leu 930 935 935 935 935 935 936 936 936 935 936 936 936 936 936 936 936 936 936 936 936 936 936 936 940 945 940 940 940 945 940 9
925 930 935 gac agc atg ggg aac ccc cgc tgc gat ggc cac cag cag ggt tac ccc 3544 Asp Ser Met Gly Asn Pro Arg Cys Asp Gly His Gln Gln Gly Tyr Pro 940 945 950
gac agc atg ggg aac ccc cgc tgc gat ggc cac cag cag ggt tac ccc 3544 Asp Ser Met Gly Asn Pro Arg Cys Asp Gly His Gln Gln Gly Tyr Pro 940 945 950
Asp Ser Met Gly Asn Pro Arg Cys Asp Gly His Gln Gln Gly Tyr Pro 940 945 950
Asp Ser Met Gly Asn Pro Arg Cys Asp Gly His Gln Gln Gly Tyr Pro 940 945 950
940 945 950
cgc aag tgg agg act gat gac gcc ccg ctc tag ggactgcagc ccagccccag 3597
Arg Lys Trp Arg Thr Asp Asp Ala Pro Leu
955 960
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organization accountable regularization realization accountable 3097
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tcagcctgcg cctgagctgc atgcgccacc atttttggca gcgtggcagc tttgcaaggg 4017

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4118

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<211> 963

<212> PRT

<213> Homo sapiens

<400> 5

Met Pro Arg Val Val Gly Pro Gly Ala Asn Leu Cys Phe Gln Val Arg

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Glu Arg Gly Ser Cys Cys Ser Ser Arg Leu Arg Leu Ala Ala Asn His 20 25 30

Ile Trp Glu Trp Pro Pro Cys Ala Pro Val Ile Thr Thr Val Ala Leu
35 40 45

Lys Gln Leu Ala Ala Leu Leu Leu Val His Val Gly Gly Phe Leu 50 55 60

Glu Pro Pro Pro Leu Ala Gly Phe Cys Leu Thr Pro Leu Ser Phe Pro 65 70 75 80

Cys Arg Leu Ser Ser Ala Asp Gly Pro Gly Ala Gly Met Ala Asp Ser 85 90 95

Ser Glu Gly Pro Arg Ala Gly Pro Gly Glu Val Ala Glu Leu Pro Gly
100 105 110

Asp Glu Ser Gly Thr Pro Gly Gly Glu Ala Phe Pro Leu Ser Ser Leu 115 120 125

Ala Asn Leu Phe Glu Gly Glu Asp Gly Ser Leu Ser Pro Ser Pro Ala



130	135	140
100	133	140

Asp	Ala	Ser	Arg	Pro	Ala	Gly	Pro	Gly	Asp	Gly	Arg	Pro	Asn	Leu	Arg
145					150					155					160

- Met Lys Phe Gln Gly Ala Phe Arg Lys Gly Val Pro Asn Pro Ile Asp 165 170 175
- Leu Leu Glu Ser Thr Leu Tyr Glu Ser Ser Val Val Pro Gly Pro Lys
 180 185 190
- Lys Ala Pro Met Asp Ser Leu Phe Asp Tyr Gly Thr Tyr Arg His His
 195 200 205
- Ser Ser Asp Asn Lys Arg Trp Arg Lys Lys Ile Ile Glu Lys Gln Pro 210 215 220
- Gln Ser Pro Lys Ala Pro Ala Pro Gln Pro Pro Pro Ile Leu Lys Val 225 230 235 240
- Phe Asn Arg Pro Ile Leu Phe Asp Ile Val Ser Arg Gly Ser Thr Ala 245 250 255
- Asp Leu Asp Gly Leu Leu Pro Phe Leu Leu Thr His Lys Lys Arg Leu 260 265 270
- Thr Asp Glu Glu Phe Arg Glu Pro Ser Thr Gly Lys Thr Cys Leu Pro 275 280 285
- Lys Ala Leu Leu Asn Leu Ser Asn Gly Arg Asn Asp Thr Ile Pro Val 290 295 300
- Leu Leu Asp Ile Ala Glu Arg Thr Gly Asn Met Arg Glu Phe Ile Asn 305 310 315 320
- Ser Pro Phe Arg Asp Ile Tyr Tyr Arg Gly Gln Thr Ala Leu His Ile 325 330 335

- Ala Ile Glu Arg Arg Cys Lys His Tyr Val Glu Leu Leu Val Ala Gln
 340 345 350
- Gly Ala Asp Val His Ala Gln Ala Arg Gly Arg Phe Phe Gln Pro Lys 355 360 365
- Asp Glu Gly Gly Tyr Phe Tyr Phe Gly Glu Leu Pro Leu Ser Leu Ala 370 375 380
- Ala Cys Thr Asn Gln Pro His Ile Val Asn Tyr Leu Thr Glu Asn Pro 385 390 395 400
- His Lys Lys Ala Asp Met Arg Arg Gln Asp Ser Arg Gly Asn Thr Val
 405 410 415
- Leu His Ala Leu Val Ala Ile Ala Asp Asn Thr Arg Glu Asn Thr Lys
 420 425 430
- Phe Val Thr Lys Met Tyr Asp Leu Leu Leu Leu Lys Cys Ala Arg Leu
 435 440 445
- Phe Pro Asp Ser Asn Leu Glu Ala Val Leu Asn Asn Asp Gly Leu Ser 450 455 460
- Pro Leu Met Met Ala Ala Lys Thr Gly Lys Ile Gly Ile Phe Gln His 465 470 475 480
- Ile Ile Arg Arg Glu Val Thr Asp Glu Asp Thr Arg His Leu Ser Arg
 485 490 495
- Lys Ser Lys Asp Trp Ala Tyr Gly Pro Val Tyr Ser Ser Leu Tyr Asp
 500 505 510
- Leu Ser Ser Leu Asp Thr Cys Gly Glu Glu Ala Ser Val Leu Glu Ile 515 520 525
- Leu Val Tyr Asn Ser Lys Ile Glu Asn Arg His Glu Met Leu Ala Val

Glu Pro Ile Asn Glu Leu Leu Arg Asp Lys Trp Arg Lys Phe Gly Ala Val Ser Phe Tyr Ile Asn Val Val Ser Tyr Leu Cys Ala Met Val Ile Phe Thr Leu Thr Ala Tyr Tyr Gln Pro Leu Glu Gly Thr Pro Pro Tyr Pro Tyr Arg Thr Thr Val Asp Tyr Leu Arg Leu Ala Gly Glu Val Ile Thr Leu Phe Thr Gly Val Leu Phe Phe Phe Thr Asn Ile Lys Asp Leu Phe Met Lys Lys Cys Pro Gly Val Asn Ser Leu Phe Ile Asp Gly Ser Phe Gln Leu Leu Tyr Phe Ile Tyr Ser Val Leu Val Ile Val Ser Ala Ala Leu Tyr Leu Ala Gly Ile Glu Ala Tyr Leu Ala Met Met Val Phe Ala Leu Val Leu Gly Trp Met Asn Ala Leu Tyr Phe Thr Arg Gly Leu Lys Leu Thr Gly Thr Tyr Ser Ile Met Ile Gln Lys Ile Leu Phe Lys Asp Leu Phe Arg Phe Leu Leu Val Tyr Leu Leu Phe Met Ile Gly Tyr Ala Ser Ala Leu Val Ser Leu Leu Asn Pro Cys Ala Asn Met Lys Val

Cys Asn Glu Asp Gln Thr Asn Cys Thr Val Pro Thr Tyr Pro Ser Cys
740 745 750

Arg Asp Ser Glu Thr Phe Ser Thr Phe Leu Leu Asp Leu Phe Lys Leu 755 760 765

Thr Ile Gly Met Gly Asp Leu Glu Met Leu Ser Ser Thr Lys Tyr Pro
770 775 780

Val Val Phe Ile Ile Leu Leu Val Thr Tyr Ile Ile Leu Thr Ser Val
785 790 795 800

Leu Leu Leu Asn Met Leu Ile Ala Leu Met Gly Glu Thr Val Gly Gln 805 810 815

Val Ser Lys Glu Ser Lys His Ile Trp Lys Leu Gln Trp Ala Thr Thr 820 825 830

Ile Leu Asp Ile Glu Arg Ser Phe Pro Val Phe Leu Arg Lys Ala Phe 835 840 845

Arg Ser Gly Glu Met Val Thr Val Gly Lys Ser Ser Asp Gly Thr Pro 850 855 860

Asp Arg Arg Trp Cys Phe Arg Val Asp Glu Val Asn Trp Ser His Trp 865 870 875 880

Asn Gln Asn Leu Gly Ile Ile Asn Glu Asp Pro Gly Lys Asn Glu Thr
885 890 895

Tyr Gln Tyr Tyr Gly Phe Ser His Thr Val Gly Arg Leu Arg Arg Asp 900 905 910

Arg Trp Ser Ser Val Val Pro Arg Val Val Glu Leu Asn Lys Asn Ser 915 920 925

Asn Pro Asp Glu Val Val Val Pro Leu Asp Ser Met Gly Asn Pro Arg 930 935 940 Cys Asp Gly His Gln Gln Gly Tyr Pro Arg Lys Trp Arg Thr Asp Asp 945 950 955 960
Ala Pro Leu

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<211> 764

<212> PRT

<213> Homo sapiens

<400> 6

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20 25 30

Gly Ser Gly Leu Pro Pro Met Glu Ser Gln Phe Gln Gly Glu Asp Arg
35 40 45

Lys Phe Ala Pro Gln Ile Arg Val Asn Leu Asn Tyr Arg Lys Gly Thr
50 55 60

Gly Ala Ser Gln Pro Asp Pro Asn Arg Phe Asp Arg Asp Arg Leu Phe
65 70 75 80

Asn Ala Val Ser Arg Gly Val Pro Glu Asp Leu Ala Gly Leu Pro Glu 85 90 95

Tyr Leu Ser Lys Thr Ser Lys Tyr Leu Thr Asp Ser Glu Tyr Thr Glu 100 105 110

Gly Ser Thr Gly Lys Thr Cys Leu Met Lys Ala Val Leu Asn Leu Lys 115 120 125

Asp Gly Val Asn Ala Cys Ile Leu Pro Leu Leu Gln Ile Asp Arg Asp

Arg Val Ser Leu Tyr Asp Leu Ala Ser Val Asp Ser Cys Glu Glu Asn Ser Val Leu Glu Ile Ile Ala Phe His Cys Lys Ser Pro His Arg His Arg Met Val Val Leu Glu Pro Leu Asn Lys Leu Leu Gln Ala Lys Trp Asp Leu Leu Ile Pro Lys Phe Phe Leu Asn Phe Leu Cys Asn Leu Ile Tyr Met Phe Ile Phe Thr Ala Val Ala Tyr His Gln Pro Thr Leu Lys Lys Gln Ala Ala Pro His Leu Lys Ala Glu Val Gly Asn Ser Met Leu Leu Thr Gly His Ile Leu Ile Leu Leu Gly Gly Ile Tyr Leu Leu Val Gly Gln Leu Trp Tyr Phe Trp Arg Arg His Val Phe Ile Trp Ile Ser Phe Ile Asp Ser Tyr Phe Glu Ile Leu Phe Leu Phe Gln Ala Leu Leu Thr Val Val Ser Gln Val Leu Cys Phe Leu Ala Ile Glu Trp Tyr Leu Pro Leu Leu Val Ser Ala Leu Val Leu Gly Trp Leu Asn Leu Leu Tyr Tyr Thr Arg Gly Phe Gln His Thr Gly Ile Tyr Ser Val Met Ile Gln

Lys Val Ile Leu Arg Asp Leu Leu Arg Phe Leu Leu Ile Tyr Leu Val

Ser	Gly	Asn	Pro	Gln	Pro	Leu	Val	Asn	Ala	Gln	Cys	Thr	Asp	Asp	Tyr
145					150					155					160
Tyr	Arg	Gly	His	Ser	Ala	Leu	His	Ile	Ala	Ile	Glu	Lys	Arg	Ser	Leu
				165					170					175	
Gln	Cys	Val	Lys	Leu	Leu	Val	Glu	Asn	Gly	Ala	Asn	Val	His	Ala	Arg
			180					185					190		
Ala	Cys	Gly	Arg	Phe	Phe	Gln	Lys	Gly	Gln	Gly	Thr	Cys	Phe	Tyr	Phe
		195					200					205			
Gly	Glu	Leu	Pro	Leu	Ser	Leu	Ala	Ala	Cys	Thr	Lys	Gln	Trp	Asp	Val
	210					215					220				
Val	Ser	Tyr	Leu	Leu	Glu	Asn	Pro	His	Gln	Pro	Ala	Ser	Leu	Gln	Ala
225					230					235					240
Thr	Asp	Ser	Gln	Gly	Asn	Thr	Val	Leu	His	Ala	Leu	Val	Met	Ile	Ser
				245					250				•	255	
Asp	Asn	Ser	Ala	Glu	Asn	Ile	Ala	Leu	Val	Thr	Ser	Met	Tyr	Asp	Gly
			260					265					270		
Leu	Leu	Gln	Ala	Gly	Ala	Arg	Leu	Cys	Pro	Thr	Val	Gln	Leu	Glu	Asp
		275					280					285			
Ile	Arg	Asn	Leu	Gln	Asp	Leu	Thr	Pro	Leu	Lys	Leu	Ala	Ala	Lys	Glu
	290					295					300				
Gly	Lys	Ile	Glu	Ile	Phe	Arg	His	Ile	Leu	Gln	Arg	Glu	Phe	Ser	Gly
305					310					315					320
Leu	Ser	His	Leu	Ser	Arg	Lys	Phe	Thr	Glu	Trp	Cys	Tyr	Gly	Pro	Val
				325					330					335	

Phe	Leu	Phe	Gly	Phe	Ala	Val	Ala	Leu	Val	Ser	Leu	Ser	Gln	Glu	Ala
545					550					555					560
Trp	Arg	Pro	Glu	Ala	Pro	Thr	Gly	Pro	Asn	Ala	Thr	Glu	Ser	Val	Glr
				565					570					575	
Pro	Met	Glu	Gly	Gln	Glu	Asp	Glu	Gly	Asn	Gly	Ala	Gln	Tyr	Arg	Gly
			580					585					590		
Ile	Leu	Glu	Ala	Ser	Leu	Glu	Leu	Phe	Lys	Phe	Thr	Ile	Gly	Met	Gly
		595					600					605			
Glu	Leu	Ala	Phe	Gln	Glu	Gln	Leu	His	Phe	Arg	Gly	Met	Val	Leu	Leu
	610					615					620				
Leu	Leu	Leu	Ala	Tyr	Val	Leu	Leu	Thr	Tyr	Ile	Leu	Leu	Leu	Asn	Met
625					630					635					640
Leu	Ile	Ala	Leu	Met	Ser	Glu	Thr	Val	Asn	Ser	Val	Ala	Thr	Asp	Ser
				645					650					655	
Trp	Ser	Ile	Trp	Lys	Leu	Gln	Lys	Ala	Ile	Ser	Val	Leu	Glu	Met	Glu
			660					665					670		
Asn	Gly	Tyr	Trp	Trp	Cys	Arg	Lys	Lys	Gln	Arg	Ala	Gly	Val	Met	Leu
		675					680					685			
Thr	Val	Gly	Thr	Lys	Pro	Asp	Gly	Ser	Pro	Asp	Glu	Arg	Trp	Cys	Phe
	690					695					700				
Arg	Val	Glu	Glu	Val	Asn	Trp	Ala	Ser	Trp	Glu	Gln	Thr	Leu	Pro	Thr
705					710					715					720

Leu Cys Glu Asp Pro Ser Gly Ala Gly Val Pro Arg Thr Leu Glu Asn

Pro Val Leu Ala Ser Pro Pro Lys Glu Asp Glu Asp Gly Ala Ser Glu

740

745

750

BI

Glu Asn Tyr Val Pro Val Gln Leu Leu Gln Ser Asn 755 760

•

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<210> 7
<211> 18
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 7
atttaggtga cactatag
                                                                    18
<210> 8
<211> 20
<212> DNA
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<220>
<223> Description of Artificial Sequence: Primer
<400> 8
taatacgact cactataggg
                                                                    20
<210> 9
<211> 19
<212> DNA
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<223> Description of Artificial Sequence: Primer
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ggaaacagct atgaccatg
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gtaaaacgac ggccagt
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<223> Description of Artificial Sequence: Primer
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aattaaccct cactaaaggg
                                                                    20
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tctacttcgg tgaactgccc
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acggcaggga gtcattcttc
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<211> 19
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<400> 14
ctgcagaact cctggcaga
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<210> 15
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<223> Description of Artificial Sequence: Primer
<400> 15
gtcaccaccg ctgtggaaaa
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<211> 21
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 16
tcctctggct tccaacccgt t
                                                                    21
<210> 17
<211> 20
<212> DNA
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Primer
<400> 17
gaactgggca gaaagtgcct
                                                                    20
<210> 18
<211> 21
<212> DNA
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Primer
<400> 18
ctggagttag ggtctccatc c
                                                                    21
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<211> 43
<212> DNA
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<211> 20
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 20
aggcccactc ggtgaacttc
                                                                   20
<210> 21
<211> 20
<212> DNA
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<223> Description of Artificial Sequence: Primer
<400> 21
gacgagcatg tacaatgaga
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```

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<212> DNA
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<223> Description of Artificial Sequence: Primer
<400> 22
gtcaccaccg ctgtggaaaa
                                                                    20
<210> 23
<211> 20
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 23
tgtggacagc tacagtgaga
                                                                    20
<210> 24
<211> 32
<212> DNA
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Primer
<400> 24
tgcactgaat tcgagcactg gtgttccctc ag
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```
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<211> 20
<212> DNA
<213> Artificial Sequence
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<223> Description of Artificial Sequence: Primer
<400> 25
tgtggacagc tacagtgaga
                                                                    20
<210> 26
<211> 19
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 26
gtggaaaacc cgaacaaga
                                                                    19
<210> 27
<211> 23
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Synthetic sequence
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                                      10
                                                          15
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Asp Ser Glu Glu Ala Ser Cys

<210> 28

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic sequence

<400> 28

Cys Gly Ser Leu Lys Pro Glu Asp Ala Glu Val Phe Lys Asp Ser Met

1 5 10 15

Val Pro Gly Glu Lys

20

 β

<210> 29

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 29

atggccacca gcagggttac

20

<210> 30

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

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<223> Description of Artificial Sequence: Primer
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                                                                    18
<210> 31
<211> 41
<212> DNA
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<220>
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<400> 31
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                                                                    41
<210> 32
<211> 20
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 32
cacctcttgt tgtcactgga
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<210> 33
<211> 23
<212> DNA
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<220>
<223> Description of Artificial Sequence: Primer
```

```
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caaatctgcg catgaagttc cag
                                                                    23
<210> 34
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 34
gccacgagaa gttccacgta gtg
                                                                    23
<210> 35
<211> 20
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: Primer
<400> 35
gctgctccca ttcttgctga
                                                                    20
<210> 36
<211> 32
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 36
```





```
<210> 37
<211> 20
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 37
atggccacca gcagggttac
                                                                    20
<210> 38
<211> 18
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 38
tctgccaggt tccagctg
                                                                    18
<210> 39
<211> 20
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Primer
<400> 39
acaagaaggc ggacatgcgg
                                                                    20
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```
<210> 40
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<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 40

atctcgtggc ggttctcaat



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1

ERROR LISTING

DATE:

12:07:35

PATENT APPLICATION

TIME:

INPUT SEQ: A:\Pg3606SEQLST.txt

L:1727 M:254 E: No. of Bases conflict, LENGTH:Input:1 Counted:20 SEQ:40

31